

Traumatic brain injury accelerates Parkinson's disease onset without altering Parkinson's neuropathology

Jonathan Spiegel^{1,2} | Je Yeong Sone³ | Tracy Butler¹ | Elizabeth Pirraglia⁴ |
Mony J de Leon¹

¹ Weill Cornell Medicine, New York, NY, USA

² Warren Alpert School of Medicine,
Providence, RI, USA

³ Pritzker School of Medicine, Chicago, IL, USA

⁴ New York University School of Medicine,
New York, NY, USA

Correspondence

Jonathan Spiegel, Weill Cornell Medicine, New
York, NY, USA

Email: jonathan_spiegel@brown.edu

Abstract

Background: Traumatic brain injury (TBI) is a well-established risk factor for Parkinson's disease (PD), though the nature of this relationship remains unclear. This study examines TBI's relationship with the AAO of and survival following PD onset among participants with PD and examines TBI's relation with PD neuropathology in an autopsy cohort.

Methods: This is a retrospective observational study using the National Alzheimer's Coordinating Centers (NACC) database. TBI status was assessed based on self-reported history. Clinicians estimate was used for determining age at onset (AAO) of cognitive decline and autopsy examination was used in assessing degree of substantia nigra neuropathology. The most recent assessment of participants was used as of June 2018, including participant visits which occurred between 2005 and 2018. The NACC dataset includes a 423 (53 TBI+) participants diagnosed with PD. Substantia nigra neuropathology was assessed in 1,133 (150 TBI+) participants, selected without regard to antemortem diagnoses.

Results: TBI was associated with a 4.9 (1.5-8.2) year earlier AAO of PD and a 5.9 (3.0-8.8) year longer survival with PD, but not with death age or severity of substantia nigra pathology.

Conclusions: TBI appears to accelerate PD onset without altering death age or PD-related neuropathology. This relationship suggests that TBI lowers the threshold required for PD pathology to present as symptomatic PD.

TABLE 1

Comparison	Difference in AAO	Hazard Ratio for PD Onset
Any TBI (n=53) vs. TBI- (n=370)	4.9 years (1.5-8.2)	1.4 (1.0-1.8)
TBI with LOC<5min (n=42) vs. TBI- (n=370)	3.6 years (-0.1-7.3)	1.2 (0.8-1.7)
TBI with LOC>5min (n=10) vs. TBI with LOC<5min (n=42)	5.5 years (-2.8-13.7)	1.8 (0.9-3.9)
TBI with LOC>5min (n=10) vs. TBI- (n=370)	9.9 years (2.7-17.0)	2.7 (1.4-5.1)

TABLE 2

	All TBI	TBI with LOC<5min	TBI with LOC>5min
OR for having substantia nigra neuron loss (moderate/severe)	0.9 (0.6-1.3), n=1133	0.7 (0.4-1.2), n=1093	0.7 (0.3-1.5) n=1014
OR for having substantia nigra hypopigmentation (moderate/severe)	0.8 (0.5-1.2), n=1133	0.7 (0.4-1.2), n=1093	0.9 (0.4-2.0) n=1014